PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/000876	28.01.2005	29.01.2004

International Patent Classification (IPC) or both national classification and IPC
C07D487/04, A61K31/495, A61P35/00

Applicant
NOVARTIS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/000876

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/000876

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-13
Industrial applicability (IA)	Yes:	Claims	1-13
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1: WO 03/037897 A (NOVARTIS AG; NOVARTIS PHARMA GMBH; BALL, HOWARD, ASHLEY; COHEN, PAMELA) 8 May 2003 (2003-05-08)
D2: WO 03/013541 A (NOVARTIS AG; NOVARTIS PHARMA GMBH; BOLD, GUIDO; CAPRARO, HANS-GEORG; C) 20 February 2003 (2003-02-20)

The present application relates to compounds of the general formula (I) (claims 1-9), the compounds (I) for use in a method of treatment (claim 9), pharmaceutical compo-sitions thereof (claim 10), the usage thereof for the preparation of a pharmaceutical composition (claims 11-12) and a process for the preparation of a compound (I) (claim 13).

The compounds (I) according to the present application are a sub-group of the compounds (I) according to D1 as well as the compounds (I) according to D2. They can be distiguished from the compounds according to ex. 1, 3 of D1 and ex. 16 of D2 only with respect to the 4-position of the piperazine-1-ylmethyl moiety which is - in the case of the known compounds - substituted by methyl or ethyl.
The compounds disclosed in D1 and D2 serve for the same medical purpose as the compounds (I) according to the present case, namely the treatment of proliferative diseases,

The novelty of claims 1-13 is acknowledged (Art. 33(2) PCT).

As closest prior art can be regarded both D1 and D2.

The problem of the present application was to provide further pyrrolopyrimidine derivati-ves which are suitable for the treatment of proliferative diseases.

This problem has been solved, as can be seen in the description

The compounds (I) have to be considered obvious for a man skilled in the art, since they are, as has already been noted above, structurally extremely close to compounds

exemplified in D1 and D2 which are employed for the same medical purpose.

Furthermore the following is noted:

The Applicant is entitled to claim all obvious modifications of what was described (cf. Guidelines C-III, 6.2); alternative variations have to be supported by a certain number of examples (s. Guidelines C-II, 4.9); in this case the breadth of the main claim represents a reasonable generalisation of what has been exemplified, so that it can be assumed that every compound falling within its scope actually provides a solution to the problem underlying the invention.

Non-limiting terms like "substituted" (without a list of specific substituents following) as used in claims 1-4 of the present application are, however, speculative in the sense of Article 33(3) PCT: They include a great variety of structural possibilities not yet explored by the applicant, the effect of which cannot be foreseen having regard to the problem underlying the present invention.

Non-limititing terms as cited above include
- chemical groups which are structurally so remote from those of the examples that the activity of molecules comprising them cannot be predicted within the limits of qualitative structure-activity-relationship considerations
- mutagenic and/or toxic groups
- known pharmacophoric groups with the same or a completely different activity which leads to hybrid molecules or bio-conjugates the actual biological activities of which are unpredictable,

i.e. it cannot be foreseen, whether those molecules provide a solution to the problem.

The applicant could - in order to overcome this objection - submit all information avail-able to substantiate that all claimed compounds are an non-obvious solution to the pro-blem underlying the application (cf. Article 33(3) PCT in conjunction with Articles 5 and 6 PCT) or, alternatively, restrict the claims concerned appropriately.

An inventive step in the sense of Article 33(3) PCT is therefore not acknowledged for the

subject-matter of claims 1-13 according to the present case.

Further objections:

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclo-sed in the document D1 is not mentioned in the description, nor is this document iden-tified therein.

The relative term "lower" used in claims 5-6 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

Each dependent claim should have a narrower scope than the claim(s) from which it depends. This requirement is not fulfilled for claim 8, as the term "isolated" is not able to narrow the scope of claim 8 with respect to the preceding claims. Hence the subject-matter of claim 8 does not fulfil the requirements of Article 6 PCT.